66. (new) The pharmaceutical composition of Claim 19, wherein the compound is Formula II,

67. (new) The pharmaceutical composition of Claim 19, wherein the compound is Formula III.

68. (new) The pharmaceutical composition of Claim 19, wherein the compound is Formula IV.

69. (new) The pharmaceutical composition of Claim 65, wherein R is H.

70. (new) The pharmaceutical composition of Claim 66, wherein R is H.

71. (new) The pharmaceutical composition of Claim 67, wherein R is H.

72. (new) The pharmaceutical composition of Claim 68, wherein R is H.

73. (new) The pharmaceutical composition of Claim 21, wherein the compound is Formula I.

74. (new) The pharmaceutical composition of Claim 21, wherein the compound is Formula II,

A7 concld

75. (new) The pharmaceutical composition of Claim 21, wherein the compound is Formula III.

76. (new) The pharmaceutical composition of Claim 21, wherein the compound is Formula IV.

77. (new) The pharmaceutical composition of Claim 73, wherein R is H.

78. (new) The pharmaceutical composition of Claim 74, wherein R is H.

79. (new) The pharmaceutical composition of Claim 75, wherein R is H.

80. (new) The pharmaceutical composition of Claim 76, wherein R is H.

Remarks

In a restriction requirement dated November 5, 2002, the Examiner required restriction under 35 U.S.C. § 121 between the following groups:

I. Claims 1-12, 17-22 drawn to a composition and method for the treatment of hepatitis B, C, and D, classified in class 514, subclass 42+.

II. Claims 13-16, drawn to a composition and method for the treatment of HIV and AIDS, classified in class 514, subclass 42+.

III. Claims 23-25, drawn to a method for the treatment of a proliferative disorder, classified in class 514, subclass 42+.

IV. Claims 26 and 27, drawn to a process for preparing a 5' pyrimidine nucleoside, classified in class 536, subclass 28.1.

V. Claims 28 and 29, drawn to a process for preparing a 5' pyrimidine nucleoside, classified in class 536, subclass 28.1.

VI. Claims 30 and 31, drawn to a process for preparing a 5' purine nucleoside, classified in class 536, subclass 27.21.

VII. Claim 32, drawn to a process for preparing a nucleoside triphosphate, classified in class 536, subclass 27.1+.

The Examiner has provided that election of one group chosen from Groups I-III will also allow for one of Groups IV-VII to be examined as well. Therefore, Applicants provisionally elect to prosecute Group I, claims 1-12 and 17-22, and Group IV, claims 26 and 27. This election is made without traverse.

Sincerely,

Sherry M. Knowles
Registration No. 33,052

by express permission
KRISTIN CHRUDIMSKY
Reg# 51,561

Enclosure: Marked up version of amendments

King & Spalding LLP
191 Peachtree Street
Atlanta, Georgia 30303
404-572-3541 (Direct Line)
404-572-5145 (Facsimile)

CERTIFICATE OF MAILING

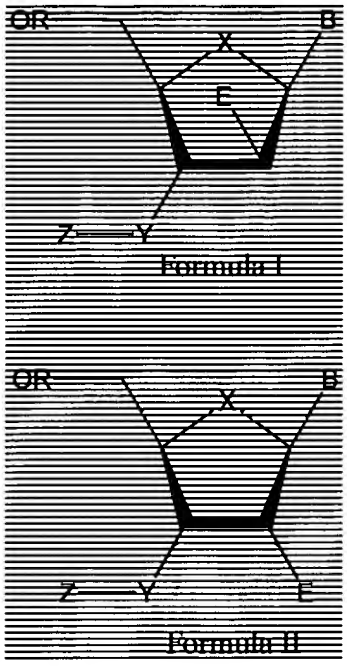
I hereby certify that this Response to Restriction Requirement along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as First Class in an envelope addressed to the Commissioner for Patents; P.O. Box 1450; Alexandria, VA 22313-1450.

Kristin Chrudimsky

Date: May 5, 2003

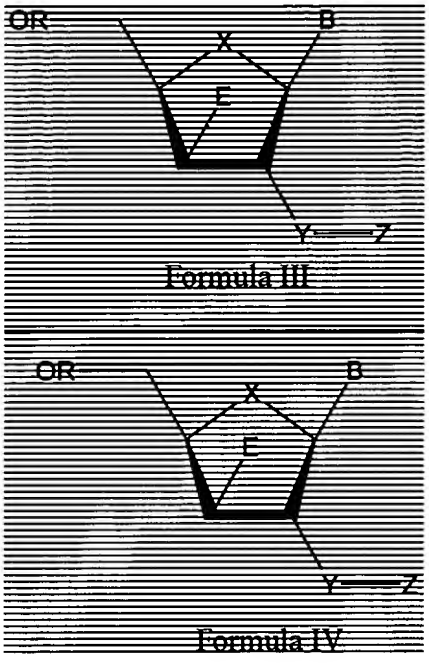
Version with Markings to Show Changes Made

1. (Once amended) A method for the treatment of hepatitis B virus (HBV) infection comprising administering an effective amount of a compound **of a formula** selected from the group consisting of formulas [I] – [IV] below and mixtures of two or more thereof:



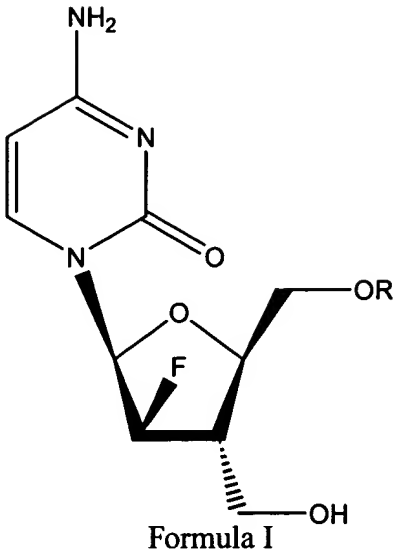
Formula I

Formula II



Formula III

Formula IV



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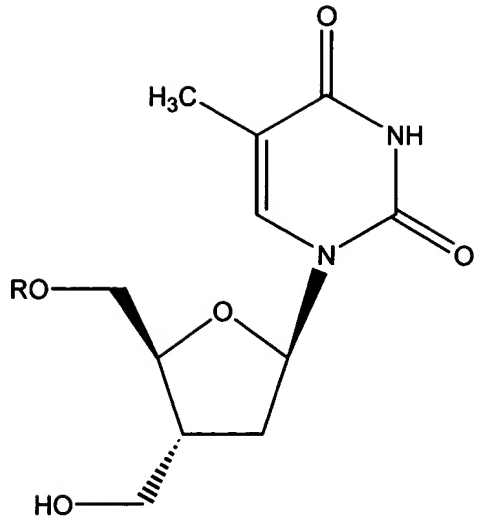

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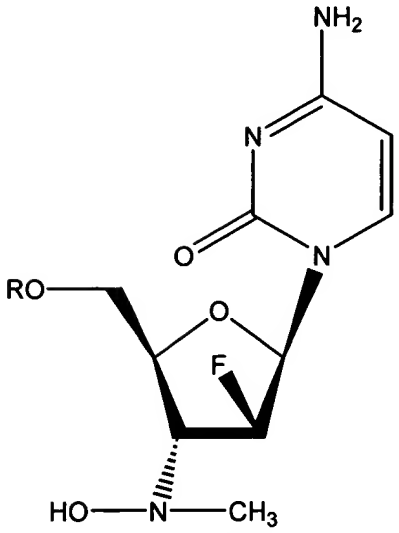
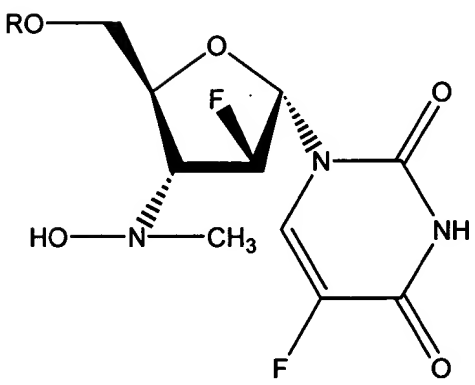


Formula III



Formula IV

wherein:

~~E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3,~~ **~~and~~** ~~F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;~~

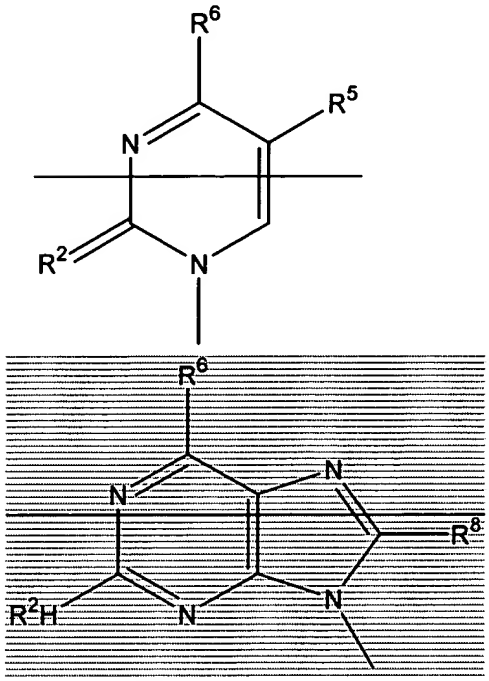
~~X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;~~

~~Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;~~

~~Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, NH_2, NHMe;~~

~~**Y-Z is either CH_2OH or $N(CH_3)OH$**~~

~~B is a base selected from the group consisting of the structure:~~

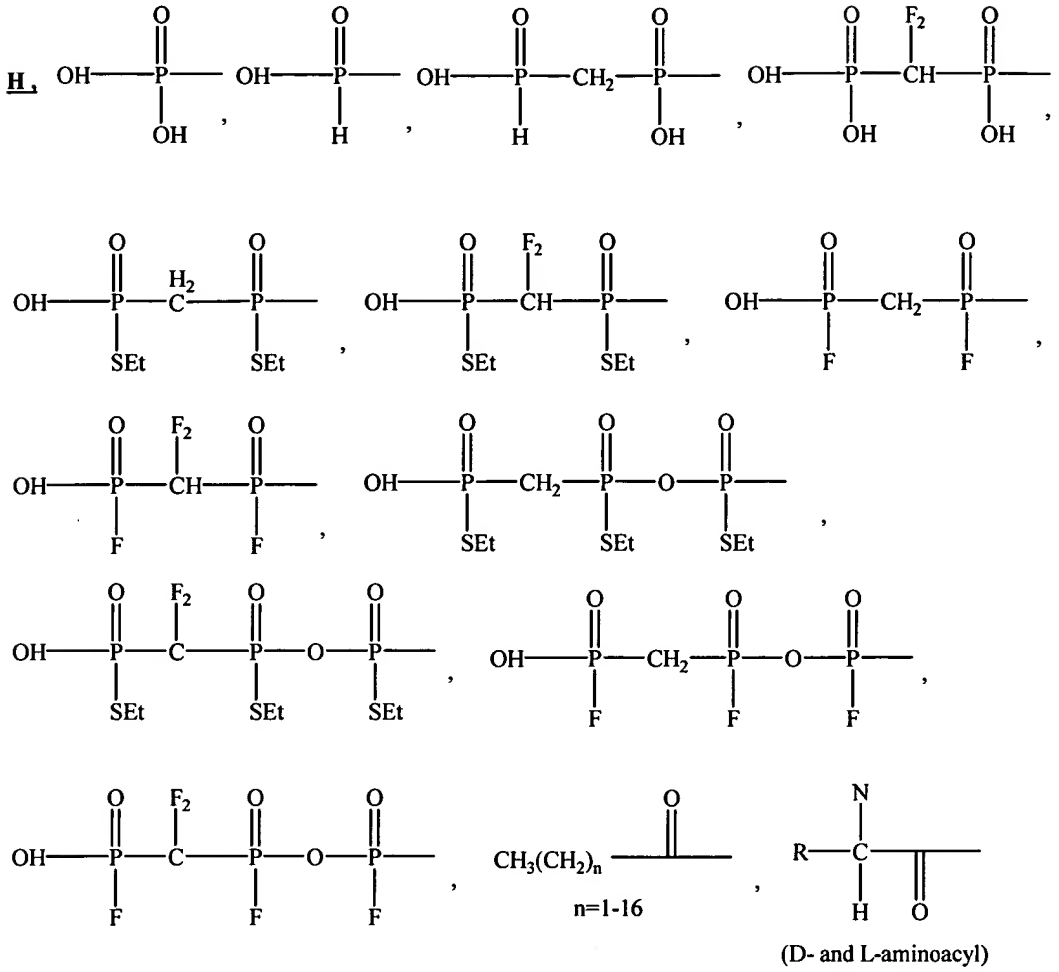


~~R^2 is selected from the group consisting of O, S, NH, NR;~~

~~R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having 1-5 carbon atoms, F, Cl, Br, I, $CH=CH_2$, CH=CHBr, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;~~

~~R^6 and R^8 are is the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe,~~ **and** ~~NMe_2; and~~

R is independently selected from the group consisting of



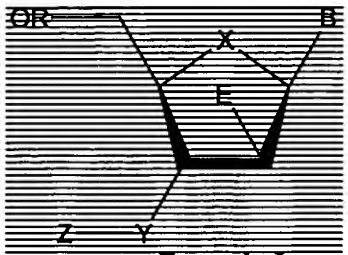
or a pharmaceutically acceptable salt or prodrug thereof, optionally in combination with a pharmaceutically acceptable carrier.

2. The method of Claim 1, further comprising administering the compound in combination or alternation with one or more additional anti-HBV agents.

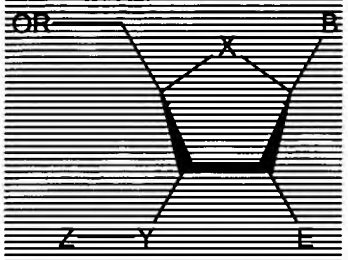
3. The method of Claim 2, wherein the additional anti-HBV agent is selected from the group consisting of FTC (the (-)-enantiomer or the racemate), L-FMAU, interferon, beta-D-dioxolanyl-guanine (DXG), beta-D-dioxolanyl-2,6-diaminopurine (DAPD), beta-D-dioxolanyl-6-chloropurine (ACP), beta-D-dioxolanyl-2-aminopurine (ADP), famciclovir, penciclovir, bis-POM PMEA (adefovir dipivoxil); lobucavir, ganciclovir, ribavarin, lamivudine (3TC), L-

thymidine (L-dT), L-2'-deoxycytidine (L-dT), L-2'-deoxycytidine-3',5'-di-O-valyl (D or L), entecavir (BMS-200475), adefovir, L-D4FC, D-D4FC, and mycophenolic acid (an IMPDH inhibitor).

5. (Once amended) A method for the treatment of hepatitis C virus (HCV) infection comprising administering an effective amount of a compound **of a formula** selected from the group consisting of formulas [I] – [IV] below and mixtures of two or more thereof:



Formula I



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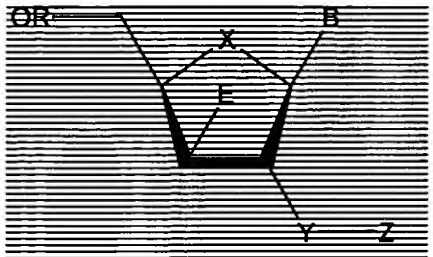
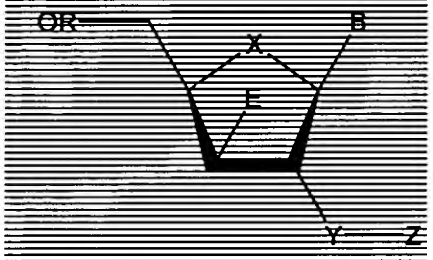
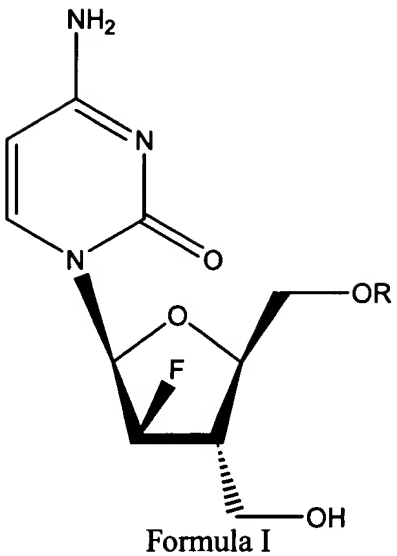


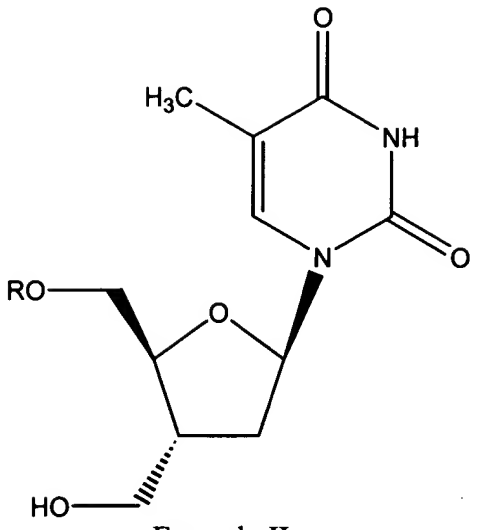
Formula III



Formula IV



Formula I



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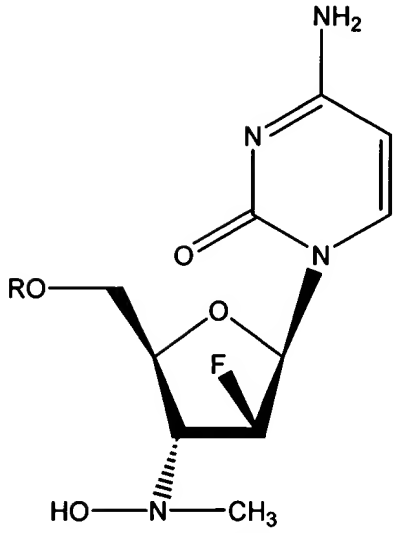
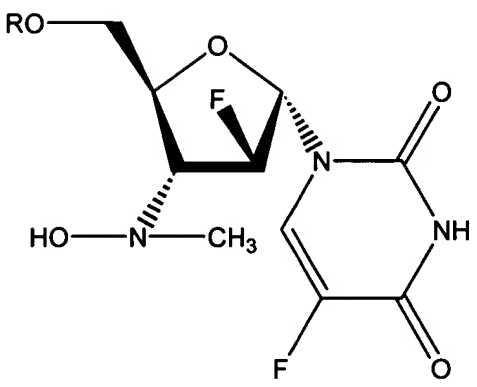


Formula III



Formula IV

wherein:

~~E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3,~~ **and** ~~F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;~~

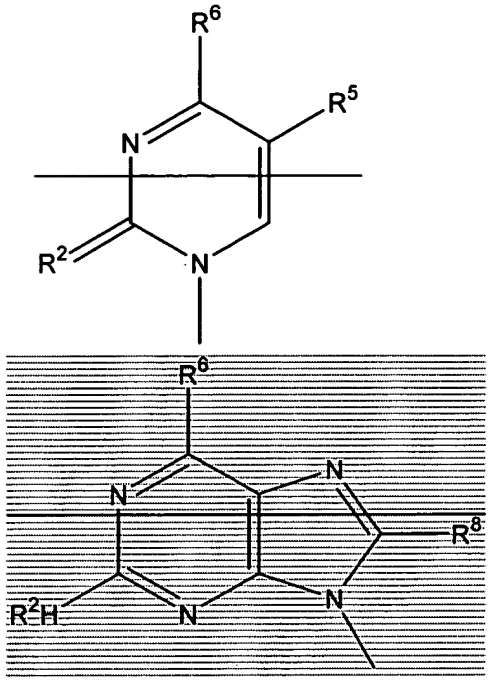
~~X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;~~

~~Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;~~

~~Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, NH_2, NHMe;~~

~~**Y-Z is either CH_2OH or $N(CH_3)OH$**~~

~~B is a base selected from the group consisting of the structure:~~

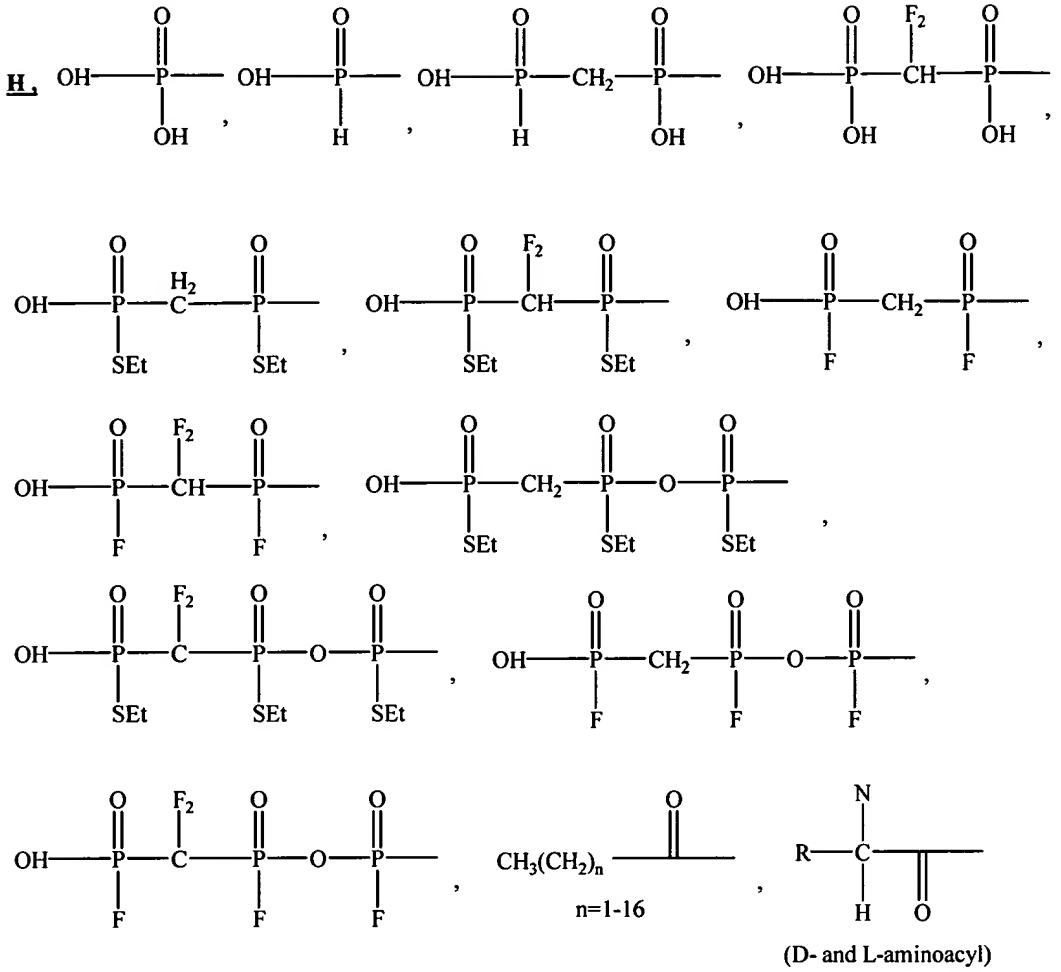


~~R^2 is selected from the group consisting of O, S, NH, NR;~~

~~R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having 1-5 carbon atoms, F, Cl, Br, I, $CH=CH_2$, CH=CHBr, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;~~

~~R^6 and R^8 are is the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe,~~ **and** ~~NMe_2; and~~

R is independently selected from the group consisting of

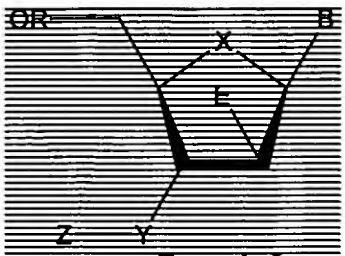


or a pharmaceutically acceptable salt or prodrug thereof, optionally in combination with a pharmaceutically acceptable carrier.

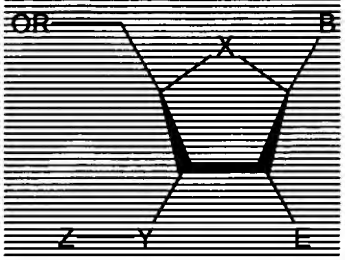
6. The method of Claim 5, further comprising administering the compound in combination or alternation with one or more additional anti-HCV agents.

7. The method of Claim 6, wherein the additional HCV agent is selected from the group consisting of interferon, macrokine, heptazyme, ribavarin (D and L), amantadine, ofloxacin, zadaxin and reticulose.

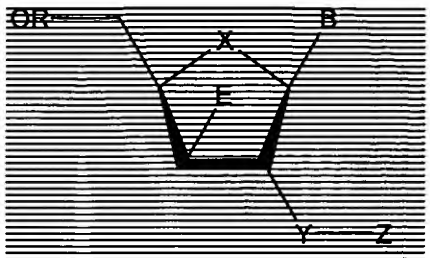
9. (Once amended) A method for the treatment of hepatitis D virus (HDV) infection comprising administering an effective amount of a compound **of a formula** selected from the group consisting of formulas [I] – [IV] below and mixtures of two or more thereof:



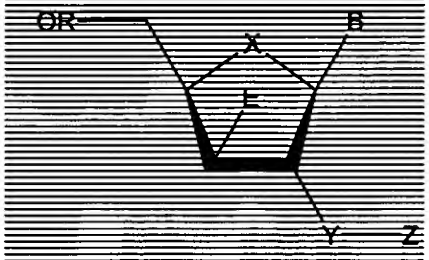
Formula I



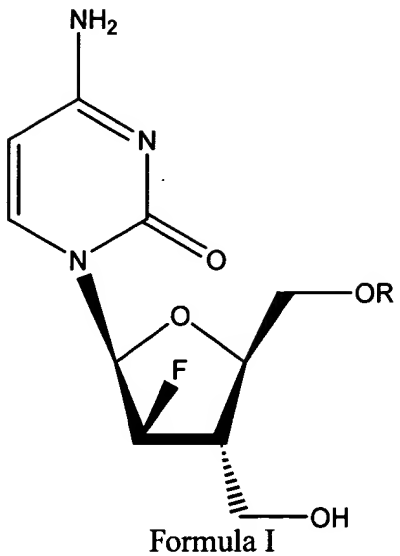
Formula II



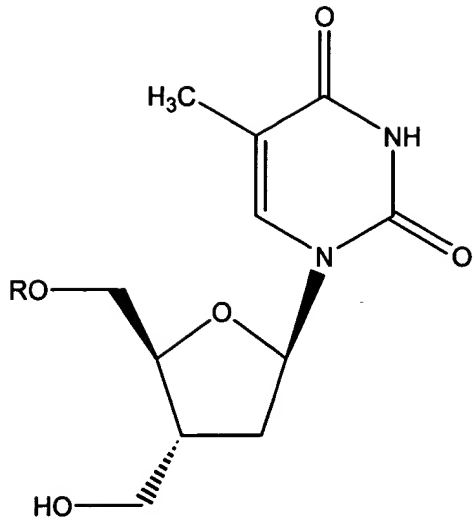
Formula III



Formula IV



Formula I



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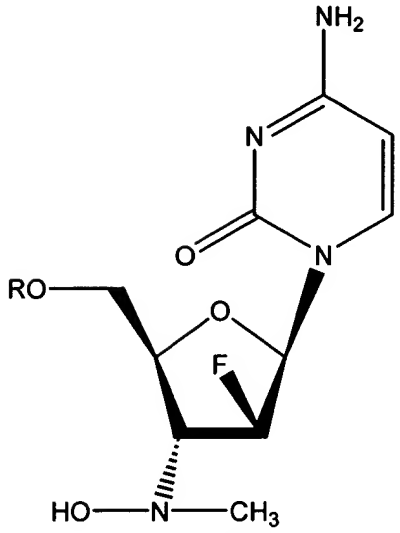
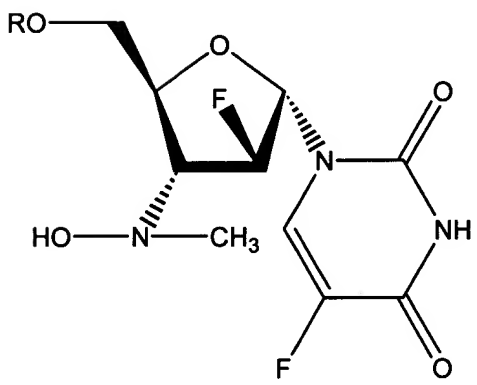


Formula III



Formula IV

wherein:

~~E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3, **and** F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;~~

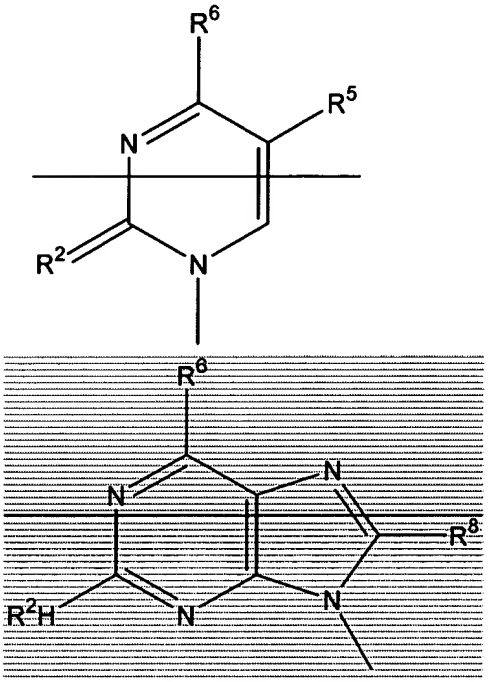
~~X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;~~

~~Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;~~

~~Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, NH_2, NHMe;~~

~~Y-Z is either CH_2OH or $N(CH_3)OH$~~

~~B is a base selected from the group consisting of the structure:~~

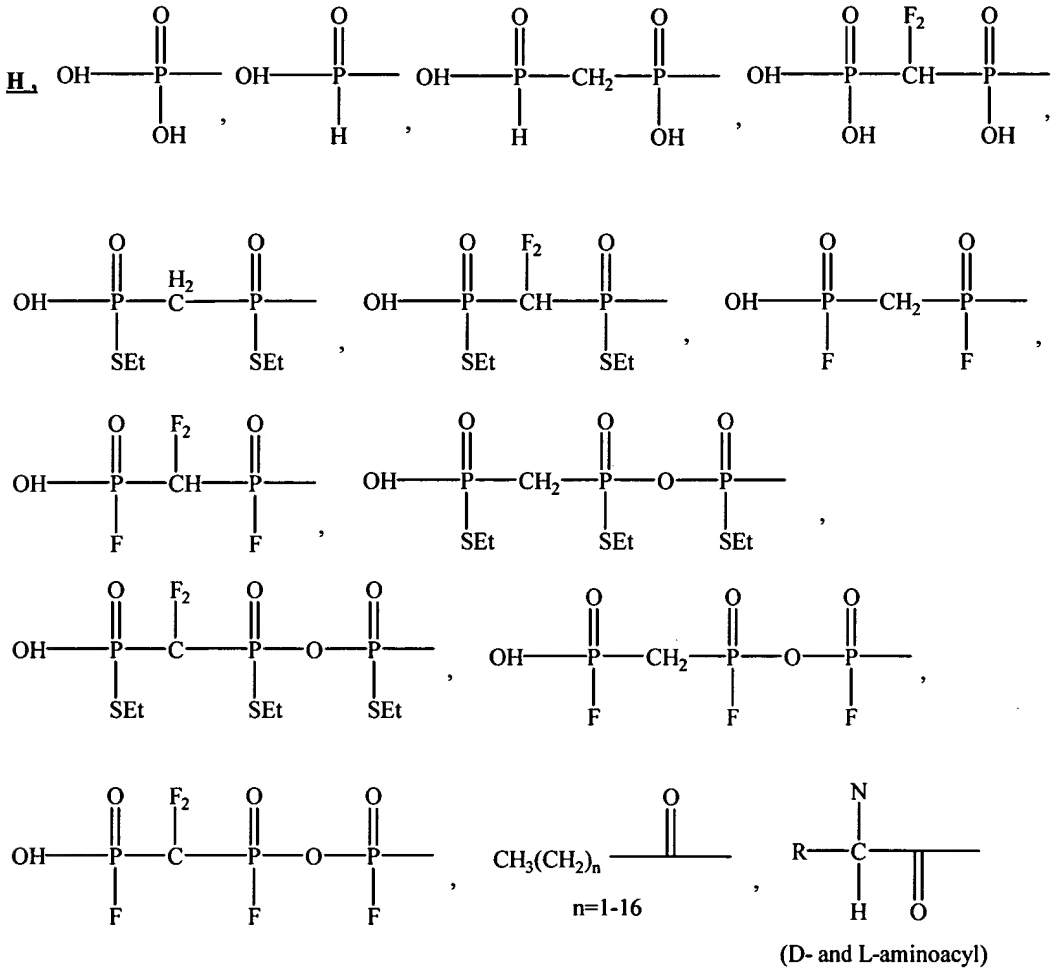


~~R^2 is selected from the group consisting of O, S, NH, NR;~~

~~R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having 1-5 carbon atoms, F, Cl, Br, I, $CH=CH_2$, CH=CHBr, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;~~

~~R^6 and R^8 are is the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe, and NMe_2; and~~

R is independently selected from the group consisting of

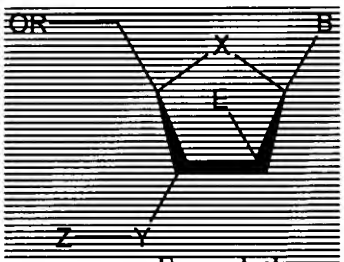


or a pharmaceutically acceptable salt or prodrug thereof, optionally in combination with a pharmaceutically acceptable carrier.

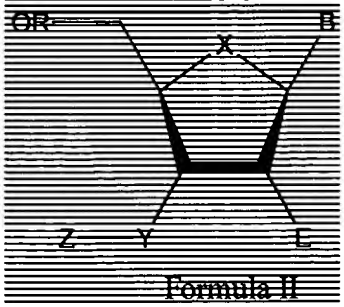
10. The method of Claim 9, further comprising administering the compound in combination or alternation with one or more additional anti-HDV agents.

11. The method of Claim 10, wherein the additional HDV agent is selected from the group consisting of FTC (the (-)-enantiomer or the racemate), L-FMAU, interferon, beta-D-dioxolanyl-guanine (DXG), beta-D-dioxolanyl-2,6-diaminopurine (DAPD), beta-D-dioxolanyl-6-chloropurine (ACP), beta-D-dioxolanyl-2-aminopurine (ADP), famciclovir, penciclovir, bis-POM PMEA (adefovir dipivoxil); lobucavir, ganciclovir, ribavarin, lamivudine (3TC), L-thymidine (L-dT), L-2'-deoxycytidine (L-dT), L-2'-deoxycytidine-3',5'-di-O-valyl (D or L), entecavir (BMS-200475), adefovir, L-D4FC, D-D4FC, and mycophenolic acid (an IMPDH inhibitor).

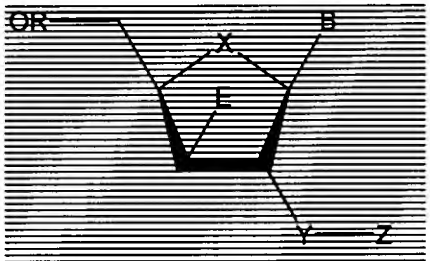
17. (Once amended) A pharmaceutical composition for the treatment of HBV comprising a combination of an effective amount of an anti-HBV agent and an effective amount of a compound **of a formula** selected from the group consisting of formulas [I] – [IV] below and mixtures of two or more thereof:



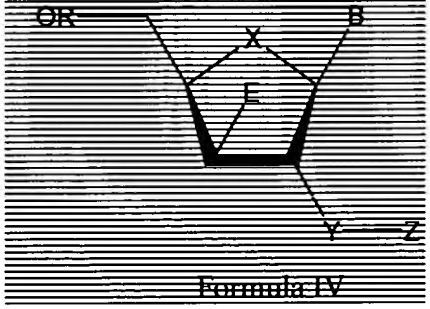
Formula I



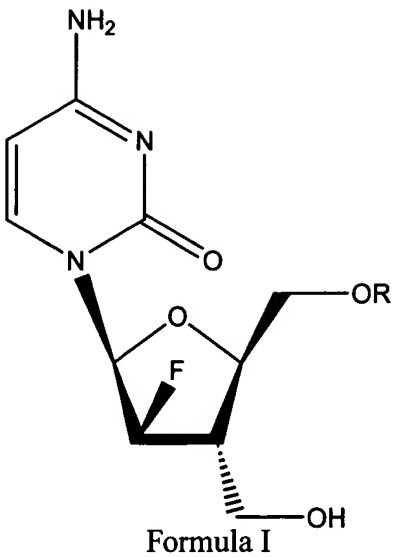
Formula II



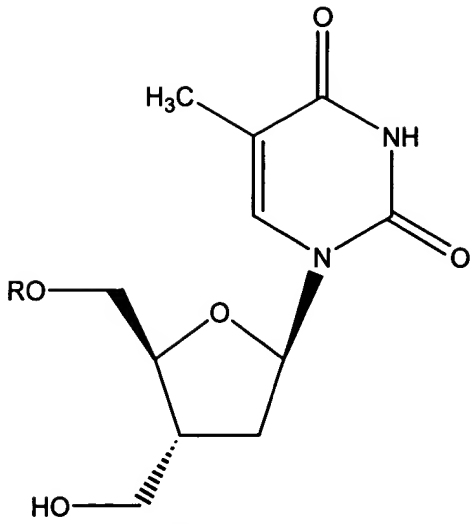
Formula III



Formula IV



Formula I



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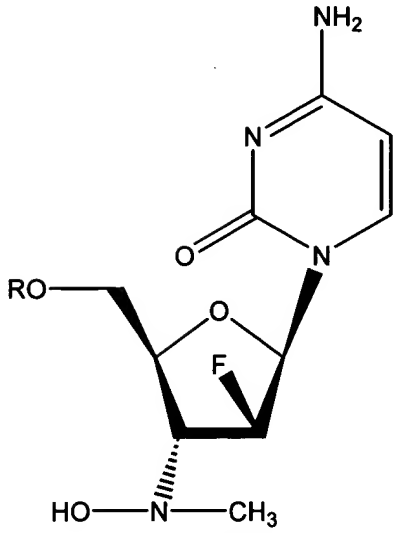
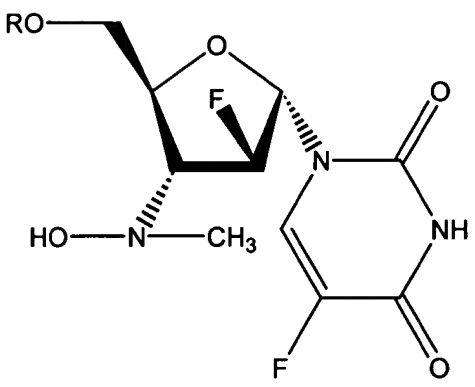


Formula III



Formula IV

wherein:

~~E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3,~~ **and** ~~F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;~~

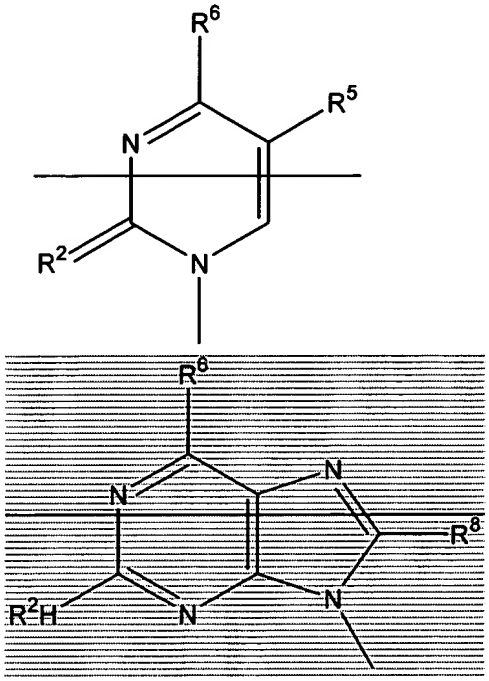
~~X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;~~

~~Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;~~

~~Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, NH_2, NHMe;~~

~~**Y-Z is either CH_2OH or $N(CH_3)OH$**~~

~~B is a base selected from the group consisting of the structure:~~

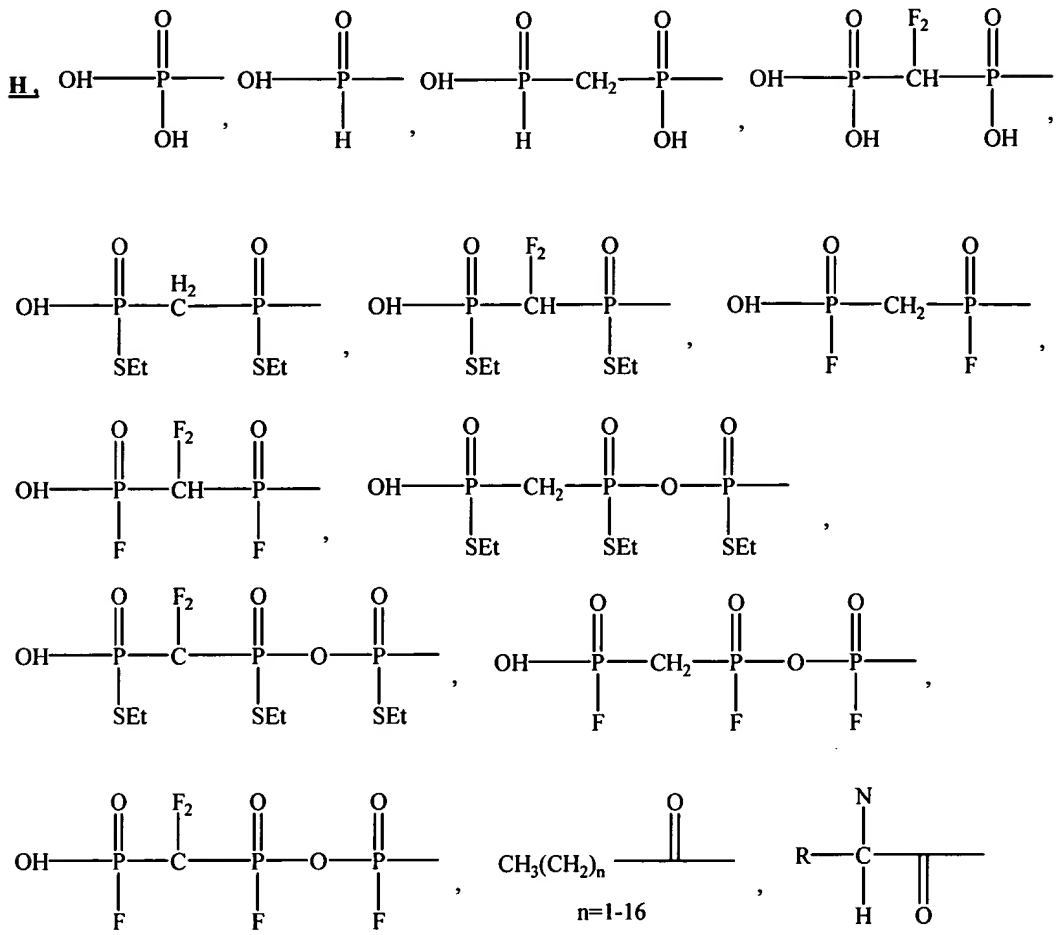


~~R^2 is selected from the group consisting of O, S, NH, NR;~~

~~R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having 1-5 carbon atoms, F, Cl, Br, I, $CH=CH_2$, CH=CHBr, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;~~

~~R^6 and R^8 are is the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe,~~ **and** ~~NMe_2; and~~

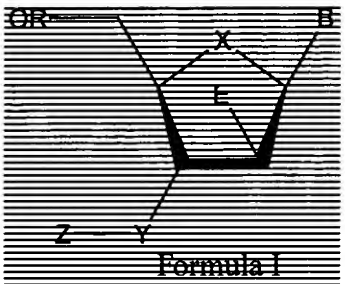
R is independently selected from the group consisting of



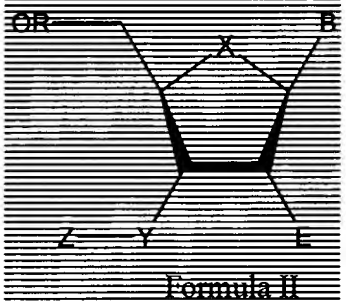
(D- and L-aminoacyl)

or a pharmaceutically acceptable salt or prodrug thereof, optionally in combination with a pharmaceutically acceptable carrier.

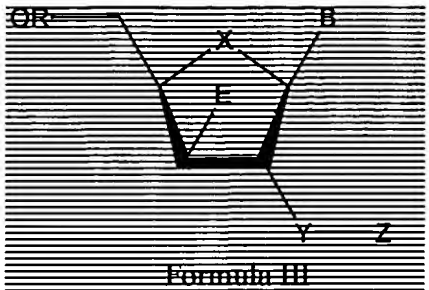
19. (Once amended) A pharmaceutical composition for the treatment of HCV comprising an anti-HCV agent and an effective amount of a compound **of a formula** selected from the group consisting of formulas [I] – [IV] below and mixtures of two or more thereof:



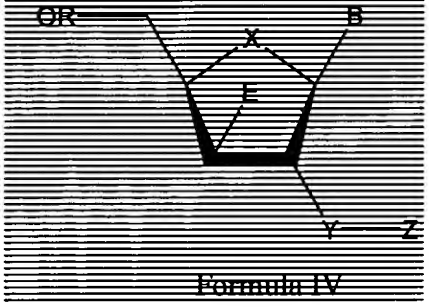
Formula I



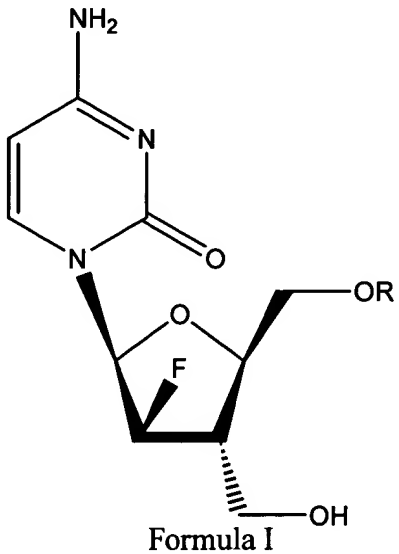
Formula II



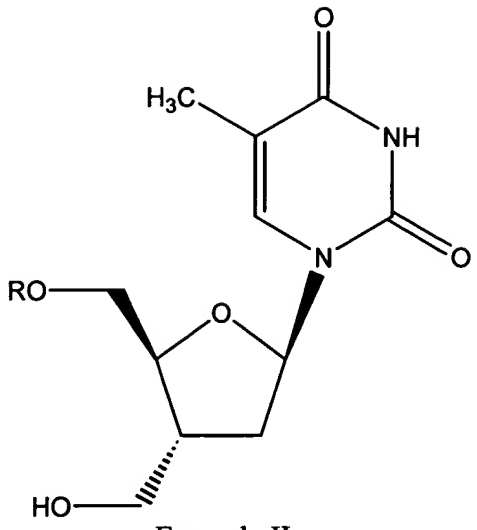
Formula III



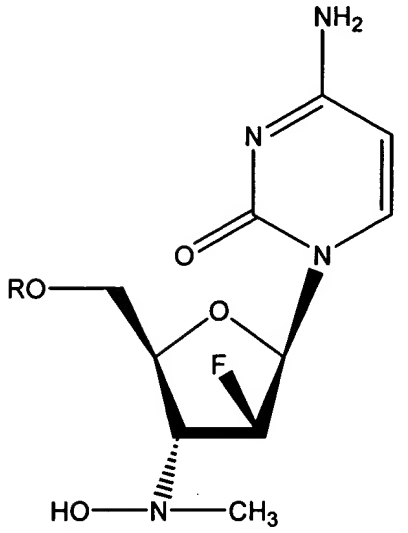
Formula IV



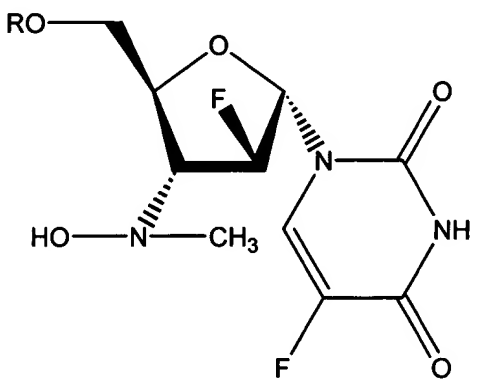
Formula I



Formula II



Formula III



Formula IV

wherein:

~~E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3, **and** F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;~~

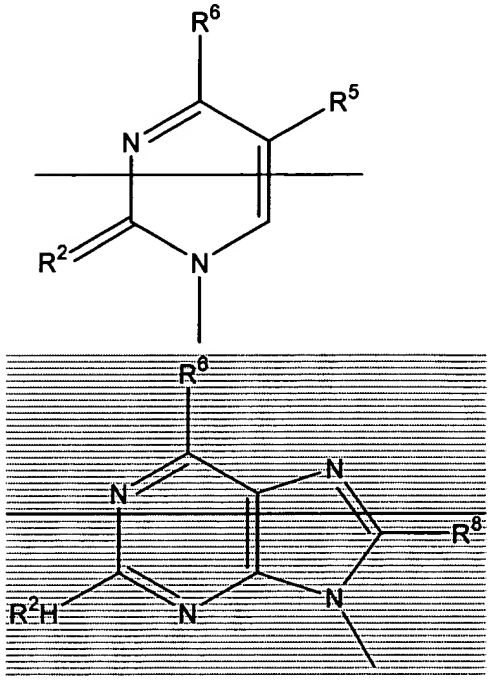
~~X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;~~

~~Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;~~

~~Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, NH_2, NHMe;~~

~~**Y-Z is either CH_2OH or $N(CH_3)OH$**~~

~~B is a base selected from the group consisting of the structure:~~

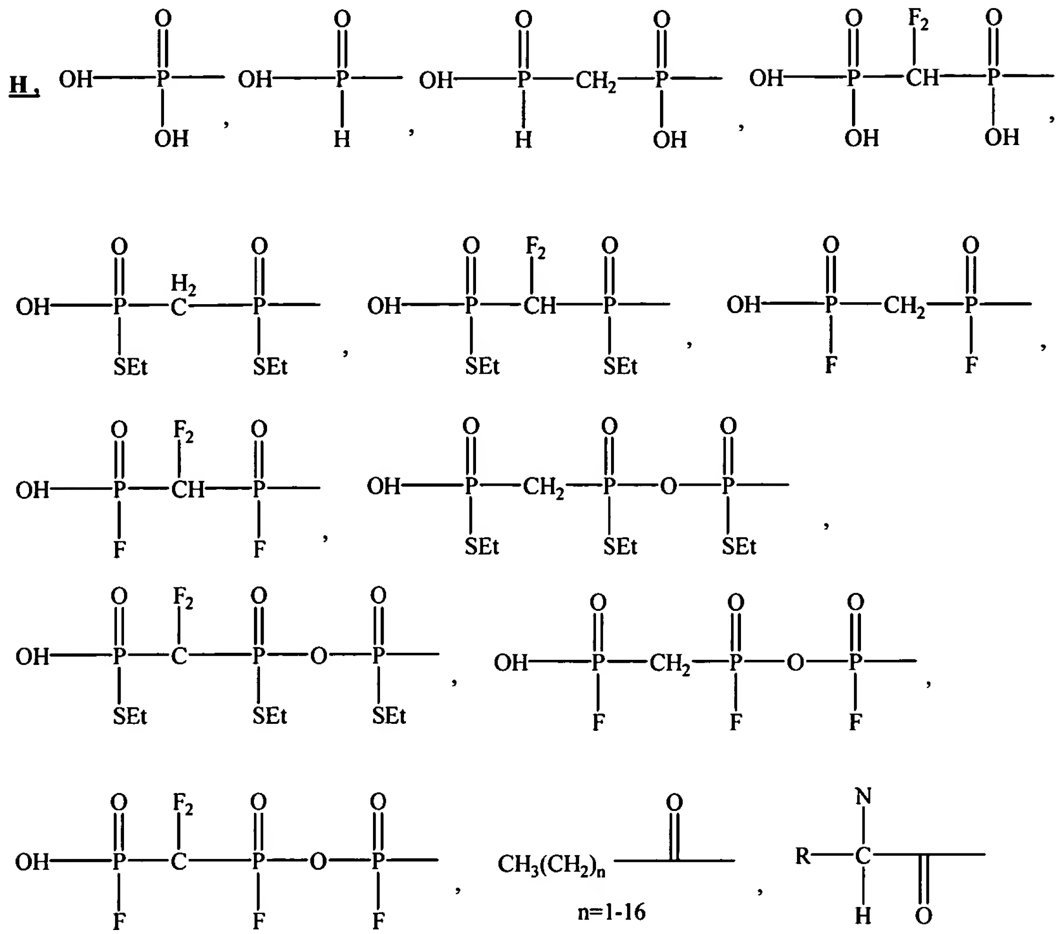


~~R^2 is selected from the group consisting of O, S, NH, NR;~~

~~R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having 1-5 carbon atoms, F, Cl, Br, I, $CH=CH_2$, CH=CHBr, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;~~

~~R^6 and R^8 are is the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe,~~ **and** ~~NMe_2; and~~

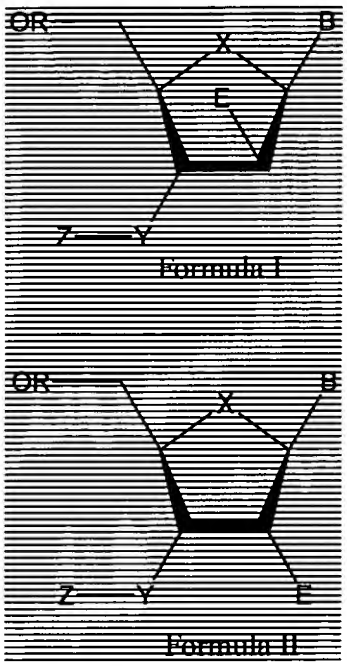
R is independently selected from the group consisting of



(D- and L-aminoacyl)

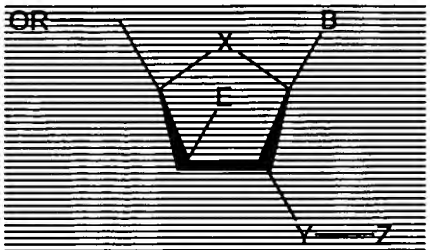
or a pharmaceutically acceptable salt or prodrug thereof, optionally in combination with a pharmaceutically acceptable carrier.

21. (Once amended) A pharmaceutical composition for the treatment of HDV comprising an anti-HDV agent and an effective amount of a compound **of a formula** selected from the group consisting of formulas [I] – [IV] below and mixtures of two or more thereof:

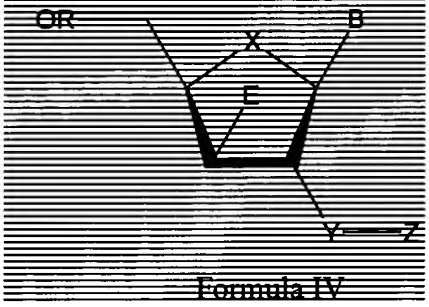


Formula I

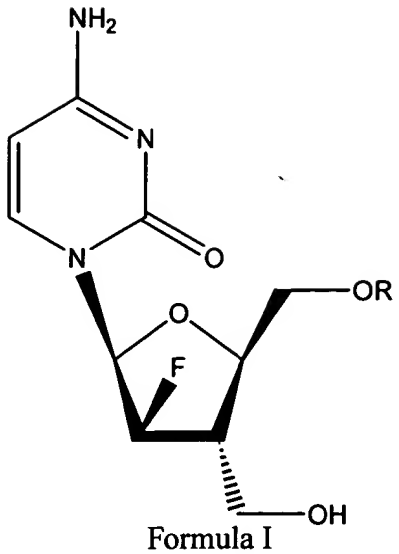
Formula II



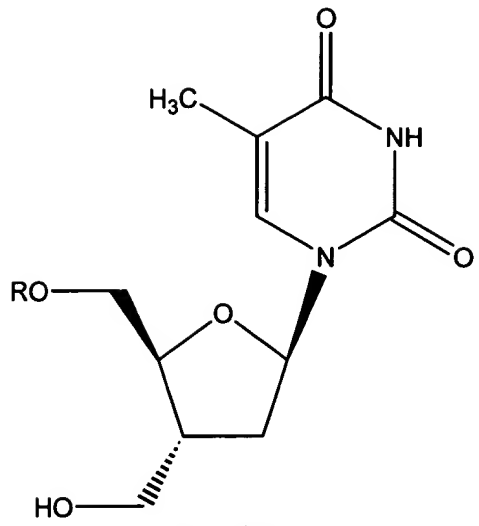
Formula III



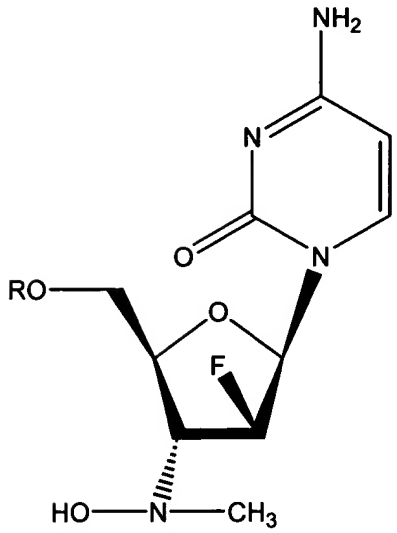
Formula IV



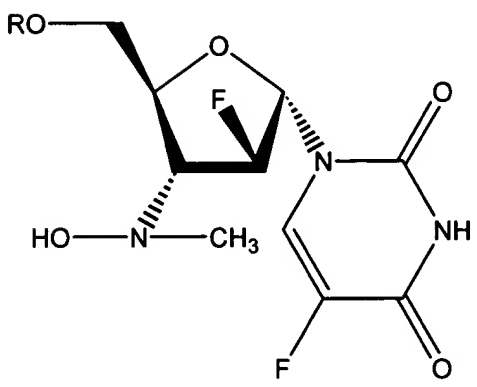
Formula I



Formula II



Formula III



Formula IV

wherein:

~~E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3,~~ **and** ~~F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;~~

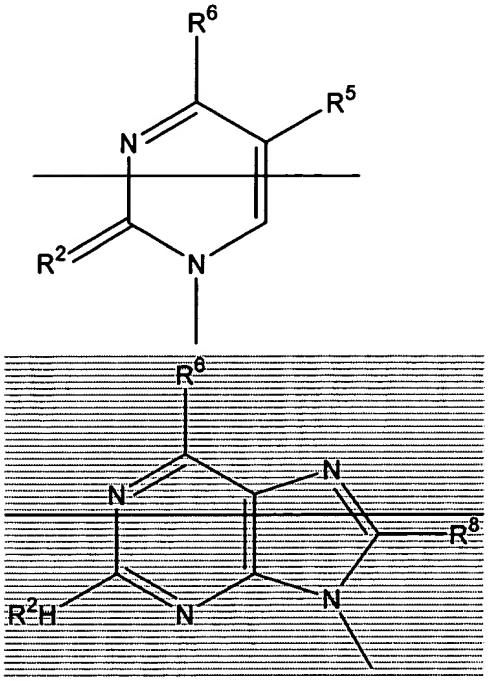
~~X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;~~

~~Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;~~

~~Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, NH_2, NHMe;~~

~~**Y-Z is either CH_2OH or $N(CH_3)OH$**~~

~~B is a base selected from the group consisting of the structure:~~

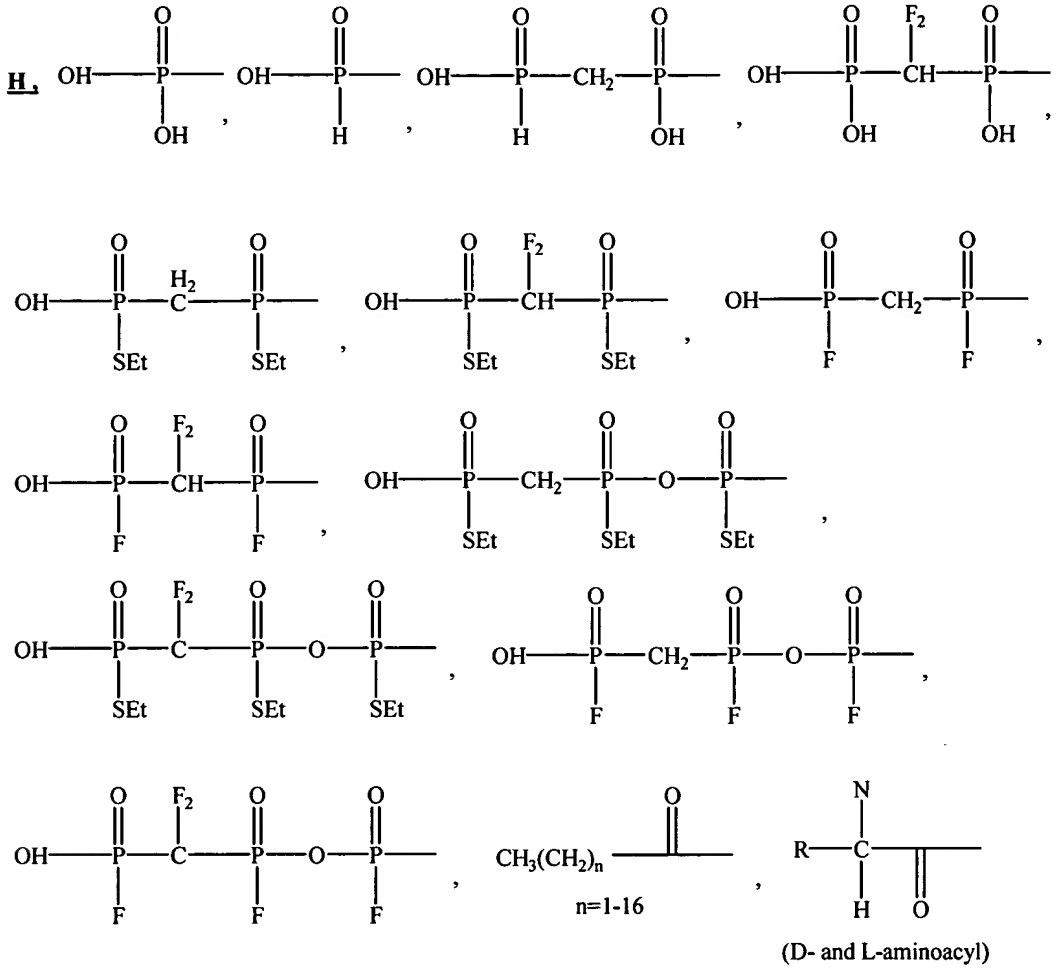


~~R^2 is selected from the group consisting of O, S, NH, NR;~~

~~R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having 1-5 carbon atoms, F, Cl, Br, I, $CH=CH_2$, CH=CHBr, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;~~

~~R^6 and R^8 are is the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe, and NMe_2; and~~

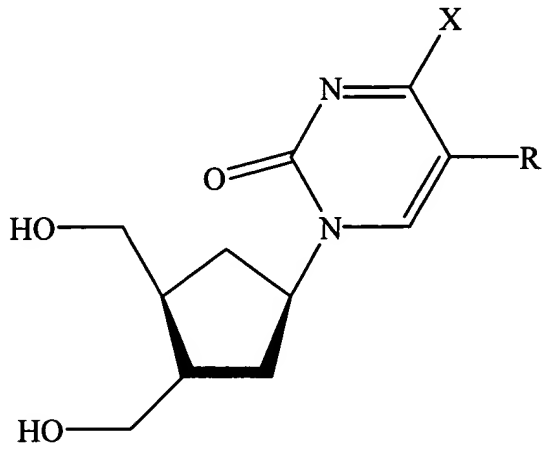
R is independently selected from the group consisting of



or a pharmaceutically acceptable salt or prodrug thereof, optionally in combination with a pharmaceutically acceptable carrier.

26. A process for stereospecifically preparing a 5'-modified pyrimidine β-nucleoside comprising

a. applying the Mitsunobu reaction to a chiral compound of the formula



b. selectively protecting the 3'-β-poxition of the resulting nucleoside of step (a) with a benzoyl protecting group or an acid labile protecting group;

c. subjecting the resulting 3'-β-protected anhydro derivative of step (b) to mild alkaline hydrolysis, followed by phosphorylating the ring-opened, 3'-β-protected product with a phosphorylating agent;

d. Saponifiction of the benzoyl group of the resulting product of step © to give the desired β-nucleoside 5'-phosphate; and

e. Optionally oxidizing the 5'-phosphate to obtain the 5'-phosphite.

27. The process of Claim 26, wherein the acid labile agent is selected from the group consisting of tetrahydropyranyl (THP), a trityl group, or dimethyl-*t*-butylsilyl (DBMS).